

# Benefit-Risk Of arterial THrombotic prEvention with Rivaroxaban for atrial fibrillation in daily clinical practice. A French cohort within the nationwide claims and hospital database (BROTHER).

**First published:** 02/08/2016

**Last updated:** 23/04/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS14567

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### Study ID

49822

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### DARWIN EU® study

No

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### Study countries

 France

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## Study description

The research question is to assess the one-year and two-year benefit-risk of rivaroxaban for stroke prevention in atrial fibrillation (SPAF) compared to vitamin K antagonists (VKA) and dabigatran among new anticoagulant users. The main objective is to compare the one-year and two-year risk of the following individual outcomes: stroke and systemic embolism (SSE), major bleeding and death, between new users of anticoagulant for SPAF during drug exposure: rivaroxaban versus VKA, and rivaroxaban versus dabigatran (standard and reduced doses). Secondary outcomes were clinically relevant bleeding (CRB), acute coronary syndrome (ACS) and a composite criterion of SSE, major bleeding or death. This is a cohort study in the French national healthcare claims and hospitalisation database (SNDS, Système National des Données de Santé) including new users of rivaroxaban, dabigatran, or VKA for SPAF with a follow-up for at least one year and up to two years per subject, and three-year history. The index date will be that of the first dispensation of rivaroxaban, dabigatran, or VKA in 2013 or 2014. Data will be extracted from 2010 to 2015. Outcomes analysis will be performed during drug exposure for matched patients on high-dimensional propensity score (hdPS), and all patients with hdPS adjustment.

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## Study status

Finalised

## Research institutions and networks

### Institutions

[Bordeaux PharmacoEpi, University of Bordeaux](#)

 France

**First published:** 07/02/2023

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**Institution**

Educational Institution

Hospital/Clinic/Other health care facility

Not-for-profit

ENCePP partner

## Contact details

### Study institution contact

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Study contact

[patrick.blin@u-bordeaux.fr](mailto:patrick.blin@u-bordeaux.fr)

### Primary lead investigator

Nicholas Moore

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Actual: 01/02/2016

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### Study start date

Actual: 24/08/2016

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### Data analysis start date

Actual: 16/11/2016

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## Date of final study report

Actual: 20/11/2018

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Bayer Pharma AG

## Study protocol

[BROTHER\\_ENCePP\\_Protocol\\_V1.0\\_20181203.pdf](#) (7.17 MB)

## Regulatory

### Was the study required by a regulatory body?

Yes

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### Is the study required by a Risk Management Plan (RMP)?

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Disease /health condition  
Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness  
Disease epidemiology  
Drug utilisation  
Effectiveness study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Main study objective:**

The main objective is to compare the one-year and two-year risk of the following individual outcomes: SSE, major bleeding and death between new users of anticoagulant for SPAF during drug exposure: rivaroxaban versus VKA, and rivaroxaban versus dabigatran (standard and reduced doses).

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

## **Anatomical Therapeutic Chemical (ATC) code**

(B01AA) Vitamin K antagonists

Vitamin K antagonists

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

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## **Medical condition to be studied**

Atrial fibrillation

## **Population studied**

### **Short description of the study population**

The study focused on subjects with a specific or sensitive diagnosis of non-valvular Atrial Fibrillation (NVAF) and a first reimbursed dispensation of rivaroxaban, dabigatran, or vitamin K antagonists in 2013 or 2014, and no previous anticoagulant dispensation in the previous three years. Two NVAF cohorts was defined: a specific cohort for main analysis to minimize the risk of false positives, and a sensitive cohort for secondary analysis to minimize the risk of false negatives.

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### **Age groups**

- Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
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## **Special population of interest**

Other

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## **Special population of interest, other**

Non valvular atrial fibrillation patients

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## **Estimated number of subjects**

150000

# Study design details

## **Outcomes**

SSE as a hospitalisation with primary diagnosis of ischemic/undefined stroke, or other systemic arterial embolism or surgical procedure for systemic arterial embolism, Major bleeding as a hospitalisation with primary diagnosis of haemorrhagic stroke or other critical organ or site bleeding, or other bleeding with blood transfusion during hospital stay, or resulting in death, All-cause of death. Composite of SSE, major bleeding and death, CRB as a hospitalisation with primary diagnosis of haemorrhagic stroke (linked or associated diagnosis also included), or other critical organ or site bleeding, or gastro-intestinal or urogenital or other bleeding, ACS as a hospitalisation with main diagnosis of myocardial infarction or unstable angina, drug use, Healthcare resources use and costs.

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## **Data analysis plan**

Statistical analysis will be carried out according to a documented and approved Statistical Analysis Plan (SAP). The SAP describes statistical analysis as foreseen at the time of planning study. Statistical analysis will be performed after database lock using SAS® software. Blind double programming will be used for main outcome measures. Primary outcomes will be analysed using survival

methods: Kaplan-Meier estimate or cumulative incidence function estimate for cumulative incidence of clinical outcomes, Cox proportional hazard risk model or Fine and Gray model to compare incidence for outcomes between rivaroxaban versus dabigatran, and rivaroxaban versus VKA (standard and reduced doses), for hdPS matched patients, and all patients with hdPS adjustment. The analysis of healthcare costs during the drug exposure will be performed as an “intent-to-treat” analysis. Costs will be estimated according to treatment group from national health insurance and collective perspectives.

## Documents

### Study results

[BROTHER\\_Study\\_report\\_1-year\\_follow-up\\_V3.0\\_Clean\\_20181120.pdf](#) (3.88 MB)

[BROTHER\\_Study\\_report\\_2-year\\_follow-up\\_V1.0clean\\_20181116.pdf](#) (4.5 MB)

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### Study publications

[Blin P, Fauchier L, Dureau-Pournin C, Sacher F, Dallongeville J, Bernard MA, La...](#)

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## Data management

### ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

## **Data sources (types)**

Administrative healthcare records (e.g., claims)

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## Data quality specifications

### **Check conformance**

Unknown

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### **Check completeness**

Unknown

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### **Check stability**

Unknown

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### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No